

2. HEALTH EFFECTS

Table 2-3. Levels of Significant Exposure to Acetone – Oral

Figure key ^a	Species (strain) No./group	Exposure parameters	Doses (mg/kg/day)	Parameters monitored	Endpoint	NOAEL (mg/kg/day)	Less serious LOAEL (mg/kg/day)	Serious LOAEL (mg/kg/day)	Effects
ACUTE EXPOSURE									
Brown and Hewitt 1984									
1	Rat 6 M	1 day 1 time/day (GO)	0, 871	HP BC OR	Hepatic Renal	871	871		Degeneration of apical microvilli in renal tubules
Charbonneau et al. 1986b									
2	Rat 6 M	1 day 1 time/day (GO)	0, 196, 588, 1,177	BC	Hepatic	1,177			
Freeman and Hayes 1985									
3	Rat 5 F	1 day 1 time/day (G)	5,370–6,980	BW GN CS	Death Bd wt Neuro		5,800 5,800	5,800 5,800	LD ₅₀ Temporary 15% loss of body weight Prostration
Kanada et al. 1994									
4	Rat (Sprague-Dawley) 4– 5 M	1 time (G)	2,438	HP	Neuro		2,438		~20% increase in a dopamine metabolite in hypothalamus
Mathias et al. 2010									
5	Rat (Wistar) 16 M	1 time (G)	7,000	BC, HP	Hepatic		7,000		77% reduction of hepatic GSH levels and 53% decrease in liver vitamin E at 24 hours
NTP 1991; Dietz et al. 1991									
6	Rat 5 M, 5 F	14 days (W)	M: 0, 714, 1,616, 2,559, 4,312, 6,942 F: 0, 751, 1,485, 2,328, 4,350, 8,560	BW OW WI GN HP CS	Hemato Hepatic Renal Other noncancer	4,312 8,560 8,560 8,560		6,942	Bone marrow hypoplasia

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Plaa et al. 1982									
7	Rat 6–7 M	1 day 1 time/day (GW)	0, 1,961	BC BI	Hepatic	1,961			
Plaa et al. 1982									
8	Rat 9–10 M	3 days 2 times/day (GW)	0, 157, 392	BC BI	Hepatic	392			
Ross et al. 1995									
9	Rat (Wistar) 6–8 F	14 days (W)	0, 90.8	BI HP	Hepatic		90		Hepatomegaly, 14% increase in liver weight
Skutches et al. 1990									
10	Rat 5–10 M	3–7 days (W)	0, 3,214	BW FI WI BI	Other noncancer		3,214		Reduced insulin stimulated glucose oxidation in epididymal fat
Valentovic et al. 1992									
11	Rat 4 M	2 days 3 times in 2 days (GW)	0, 1,766	FI WI OR UR	Renal Other noncancer	1,766 1,766			
EHRT 1987									
12	Mouse 50 F	10 days GDs 6–15 1 time/day (GW)	0, 3,500	BW CS RX DX	Bd wt Repro Develop	3,500		3,500 3,500	Reduced reproduction index, increased gestation duration Decreased survival of pups
Jeffery et al. 1991									
13	Mouse 4 F	10 days <i>ad libitum</i> (W)	0, 1,900	HP BI	Hepatic	1,900			

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NTP 1991; Dietz et al. 1991									
14	Mouse 5 M, 5 F	14 days (W)	M: 0, 965, 1,579, 3,896, 6,348, 10,314 F: 0, 1,569, 3,023, 5,481, 8,804, 12,725	BW OW WI GN HP CS	Hepatic Renal Other noncancer	1,579 12,725 12,725	3,896		Minimal to mild hepatocellular hypertrophy
Tanii et al. 1986									
15	Mouse 4 M	Once (G)	NS	LE	Death			5,250	LD ₅₀
Striegel and Carpenter 1961									
16	Guinea pig NS M	Once (G)	NS	LE	Death			3,687	LD ₅₀
INTERMEDIATE EXPOSURE									
American Biogenics Corp. 1986									
17	Rat 10 M, 10 F	46–47 days 1 time/day (GW)	0, 100, 500, 2,500	BW FI GN BC CS UR HE	Hemato Hepatic Neuro Other noncancer	500 500 500 2,500	2,500 2,500 2,500		Increased hemoglobin, hematocrit, mean cell volume Increased serum alanine aminotransferase Excessive salivation
American Biogenics Corp. 1986									
18	Rat 20 M, 20 F	93–95 days 1 time/day (GW)	0, 100, 500, 2,500	BW OW FI GN HP CS UR HE	Resp Cardio Gastro	2,500 2,500 2,500			

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					Hemato	500	2,500		Increased hemoglobin, hematocrit, mean cell hemoglobin, mean cell volume, decreased platelets
					Musc/skel	2,500			
					Hepatic	500	2,500		Increased serum alanine aminotransferase
					Renal	100	500		Increased severity of age-related nephropathy in males
					Dermal	2,500			
					Neuro	500	2,500		Decreased brain weight, salivation
					Other noncancer	2,500			
Ladefoged et al. 1989									
19	Rat 11 M	6 weeks (W)	0, 650	BW GI WI OR NX	Neuro		650		Decreased motor nerve conduction velocity
					Other noncancer	650			
Larsen et al. 1991									
20	Rat 10 M	6 weeks (W)	0, 1,071	HP CS RX	Repro	1,071			
NTP 1991; Dietz et al. 1991									
21	Rat 10 M, 10 F	13 weeks (W)	M: 0, 200, 900, 3,400 F: 0, 300, 1,200, 3,100	BW OW WI GN HP CS HE	Repro	3,100 F			
						200 M		3,400 M	11.7% decreased sperm motility

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NTP 1991; Dietz et al. 1991									
22	Rat 10 M, 10 F	13 weeks (W)	M: 0, 200, 400, 900, 1,700, 3,400 F: 0, 300, 600, 1,200, 1,600, 3,100	BW OW WI GN HP CS HE	Resp Cardio Gastro Hemato Musc/skel Hepatic Renal Dermal Neuro Other noncancer	3,400 3,400 3,400 200 ^b 3,400 3,400 900 3,400 3,400 3,400	 400 1,700	 Mild macrocytic anemia Increased incidence and severity of nephropathy in males	
Spencer et al. 1978									
23	Rat 3 NS	12 weeks <i>ad libitum</i> (W)	0, 732	BW WI HP CS	Neuro Other noncancer	732 732			
NTP 1991; Dietz et al. 1991									
24	Mouse 10 M, 10 F	13 weeks (W)	M: 0, 380, 1,353, 4,858 F: 0, 892, 4,156, 11,298	BW OW WI GN HP CS HE	Repro	11,298 F 4,858 M			

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NTP 1991; Dietz et al. 1991									
25	Mouse 10 M, 10 F	13 weeks (W)	M: 0, 380, 611, 1,353, 2,258, 4,858 F: 0, 892, 2,007, 4,156, 5,954, 11,298	BW OW WI GN HP CS HE	Resp Cardio Gastro Hemato Musc/skel Hepatic Renal Dermal Neuro Other noncancer	11,298 11,298 11,298 11,298 11,298 11,298 11,298 11,298 11,298 11,298			
Woolhiser et al. 2006									
26	Mouse (CD-1) 8 M	28 days (W)	121, 621, 1,144	BC	Immuno	1,144			

^aThe number corresponds to entries in Figure 2-3.

^bUsed to derive an intermediate-duration oral minimal risk level (MRL) of 0.6 mg/kg/day calculated using benchmark dose analysis. The BMDL_{1SD} of 57 mg/kg/day was divided by an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability). Highlighted rows indicate an MRL principal study. See Appendix A for details.

BC = blood chemistry; Bd wt or BW = body weight; BI = biochemical changes; Cardio = cardiovascular; CS = clinical signs; Develop = developmental; DX = developmental toxicity; F = female(s); FI = food intake; (G) = gavage-not specified; (GO) = gavage-oil; (GW) = gavage-water; Gastro = gastrointestinal; GD = gestation day; GN = gross necropsy; HE = hematology; Hemato = hematological; HP = histopathological; Immuno = immunological; LD₅₀ = lethal dose, 50% death; LE = lethality; LOAEL = lowest-observed-adverse-effect level; M = male(s); Musc/skel = musculoskeletal; Neuro = neurological; NOAEL = no-observed-adverse-effect level; NS = not specified; NX = neurotoxicity; OW = organ weight; Repro = reproductive; Resp = respiratory; RX = reproductive toxicity; UR = urinalysis; (W) = water; WI = water intake